## REMARKS

Claims 29 and 45-49 are pending in the present application. Claims 30-31 have been cancelled. Claim 29 has been amended and claims 45-49 have been added. Support for the addition of claim 48, can be found *e.g.* in Table 1, page 69, row 3, column 11. No new matter has been added. The claims have been rejected for lack of utility, lack of enablement, and indefiniteness.

## IDS

Applicants acknowledge that Document C29 of Paper 14, filed March 4, 2002, has not been considered by the Examiner.

Applicants also apologize that a legible copy of each reference listed in the IDS's filed as Papers 12 and 15 were not included with the IDS's. For the convenience of the Examiner, copies of the 1449's and corresponding references for these IDS's have been included as Exhibit A with this response.

## CLAIM REJECTIONS

***Rejection under 35 U.S.C. 112, Second Paragraph***

Claims 29-31 have been rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. Claims 30 and 31 have been cancelled, so this rejection is moot with respect to these claims. Applicants traverse the rejection with respect to amended claim 29.

Claim 29 has been rejected under 35 U.S.C. 112, second paragraph as being indefinite for reciting "polymorphic nucleic acid sequence comprising SEQ ID NO:400" and thus it is unclear what the metes and bounds of the invention are. Claim 29 has been amended herein to delete "one or more amino acid residues" and read only on SEQ ID NO:400. Therefore, this rejection should be withdrawn.

***Rejection under 35 U.S.C. 112, First Paragraph (New Matter)***

Claims 29-30 have been rejected under 35 U.S.C. 112, first paragraph, for containing subject matter which as not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor has possession of the invention at the time of filing. Specifically, the Examiner alleges that there is no support for the amendment to claim 29 which recites that the polymorphism may be a thymidine or a cytosine. Applicants traverse.

Applicants refer the Examiner to page 3, lines 7-10 of the specification. Here, the Applicants teach that the polymorphic site in the polymorphic sequence includes a nucleotide other than the nucleotide listed in Table 1, column 5, in this case, G. Thus, there is support in the specification, as filed, for the amendment to claim 29. Further, for clarification purposes, claim 29 has been amended herein to read wherein the nucleotide at position 26 is an adenosine, cytosine, or thymidine. Therefore, Applicants request that this rejection be withdrawn.

***Rejection under 35 U.S.C. 101***

Claims 29-31 are rejected under 35 U.S.C. 101 for lack of utility. According to the Examiner, the instant application does not correlate the presence or absence of the polymorphism of SEQ ID NO:400 with any specific use. (*See*, Office Action at pages 5-6). Claims 30 and 31 have been canceled herein. This rejection is therefore moot in regard to these claims. Applicants submit that amended claim 29 and new claims 45-49 are supported by at least one substantial, specific, and credible utility, as discussed below.

Applicants assert that the polypeptides of the pending claims have a substantial utility in the fields such as forensic medicine, population genetics, and paternity testing. (*See,* specification at page 6, lines 15-23; page 8, line 5 to page 9, line 9; page 28, lines 10-29, page 29, lines 1-26; and page 31, line 5 to page 32, line 7.).

SNPs are critical to the field of forensic medicine. (*See,* specification at page 29, line 15 to page 31, line 4). The polypeptides of the present invention, containing a polymorphic site, are of particular utility for several reasons. Since the encoded polypeptide sequences of SEQ ID NO:400, SNPs or compliments thereof were previously unidentified, they represent novel markers that can be used to separate subpopulations that cannot be distinguished on the basis of other known SNP loci. Thus, the polymorphic polypeptide sequences encoded by SEQ ID NO:400, SNPs or compliments thereof can be used to identify individuals who are differentiated

by the disclosed polymorphism. This has further utility in assessing the success of organ transplantation and *in vitro* fertilization.

Moreover, the polymorphic polypeptide sequences encoded by SEQ ID NO:400, SNPs or compliments thereof also have a credible and specific utility in paternity testing to separate and identify individuals who have the claimed polymorphism. (*See,* specification at page 31, line 5 to page 32, line 7).

Data generated by the polymorphic polypeptide sequences encoded by SEQ ID NO:400, SNPs or compliments thereof has utility beyond forensic or paternity identification. They have a credible utility in the field of population genetics. They can also be used to reconstruct the past migration history of modern humans who possess the polymorphism. Populations of the same species in different geographical regions tend to differ genetically. Such differences may in part reflect their adaptation to different environments, or they may simply be the result of change events in the evolutionary histories of the populations since the divergence. SNPs analysis tools, including the claimed polymorphic polypeptide sequences encoded by SEQ ID NO:400, SNPs or compliments thereof, can be used to describe the nature of genetic differentiation that is observed in real populations, and to understand the mechanisms for it.

Accordingly, Applicants submit that one skilled in the art would recognize the specific, real world utilities of the polymorphic polypeptide sequences encoded by SEQ ID NO:400, SNPs or compliments thereof of the present invention, in the fields of forensics, paternity testing, and population genetics. Thus, contrary to the Examiner's contention, the polymorphic polypeptide sequences encoded by SEQ ID NO:400, SNPs or compliments thereof do have an art-recognized specific, substantial, and credible utility. Therefore, Applicants respectfully request that this rejection should be withdrawn.

***Rejection under 35 U.S.C. 112, First Paragraph***

Claims 29-31 have been rejected under 35 U.S.C. 112, first paragraph, for containing subject matter which was not described in the specification in such a way to enable one skilled in the art to use the invention without undue experimentation because the invention is not supported by a specific and substantial utility. Applicants traverse for the reasons put forth above. Therefore, Applicants request that this rejection be withdrawn.

Claim 30 has been rejected under 35 U.S.C. 112, first paragraph for containing subject matter which was not described in the specification in such a way to convey to one skilled in the art that the inventors has possession of the invention at the time of filing of the instant application. Specifically, the Examiner alleges that claim 30 encompasses polypeptides that are translated in the same open reading frame as the wild type. Claim 30 has been cancelled and claims 45-49 have been added. Applicants traverse this rejection insofar as it applies to claims 45-49.

The specification discloses that the polymorphic nucleotide sequence of SEQ ID NO:400 was identified in expressed genes in a population of humans. Pending claims 29 and 45-49 are directed to an isolated polypeptide that includes a polymorphic site, where the polypeptide is encoded by polynucleotides comprising the polymorphic nucleotide sequences of SEQ ID NO:400, single nucleotide polymorphisms (SNPs) thereof (*e.g.*, adenosine, thymidine, or cytosine at position 26 of SEQ ID NO:400) or a compliment thereof.

Applicants contend that the disclosure of the nucleic acid sequence of SEQ ID NO:400 and SNPs thereof inherently discloses the amino acid sequences for the polypeptide encoded thereby as well as its compliment and proteins encoded thereby (*See,* specification at Table 1). Moreover, the specification describes the translation of the open reading frame of the nucleic acid sequence into amino acid sequences (*See,* specification at page 7, lines 6-9; page 24, lines 1-4; and page 32, lines 8 -18). Because a given nucleic acid sequence can contain only three potential open reading frames encoded by the forward (or plus) strand and three potential open reading frames encoded by the reverse (or minus) strand, one of ordinary skill in the art would readily be able to obtain the polypeptide sequences encoded by SEQ ID NO:400, SNPs or compliments thereof. The specification also demonstrates that a SNP at position 26 of SEQ ID NO: 400, *e.g.*, a substitution of thymidine for cytosine (SEQ ID NO:400), results in no change to the polypeptide encoded by SEQ ID NO:400.

***Rejection under 35 U.S.C. 102***

Claims 29 and 30 have been rejected under 35 U.S.C. 102 for anticipation in light of Nakamura, Japanese Application No. 1994092995, (the "'1994 application"). Examiner asserts that the '1994 application discloses a sequence that is identical to SEQ ID NO:400 except at position 26, wherein the nucleotide in the '1994 application sequence is a guanosine (*See* the

ClustalW alignment of SEQ ID NO:400 with the "'1994 app." sequence shown in Exhibit B, attached). Examiner further alleges that because the complement to this '1994 application sequence would have a nucleotide other than a guanosine at position 26, in this case, a cytosine, that this '1994 application sequence, therefore, somehow anticipates the sequence of SEQ ID NO:400 as claimed. Applicants traverse.

Claim 29 specifies that the nucleotide at position 26 of SEQ ID NO:400 must be an adenosine, thymidine, or cytosine. Claim 29 does not specify that the complementary nucleotide at this position must be an adenosine, thymidine, or cytosine. While it would be known to one of ordinary skill in the art what the sequence of the complementary polynucleotide of SEQ ID NO:400 would be, they would also know that this complementary polynucleotide is not itself identical to SEQ ID NO:400 (*See* the ClustalW alignment of SEQ ID NO:400 with the "'1994 app. comp." complementary sequence shown in Exhibit B, attached). Therefore, Applicants request that this rejection be withdrawn.

Claims 29 and 31 have been rejected under 35 U.S.C. 102 for anticipation in light of Nakamura, Japanese Application No. JP 0602995-A, (the "'060 application"). Examiner asserts that the sequence shown in "Result 1" (*See* page 10 of the Office Action) is the complement of SEQ ID NO:400. Applicants traverse.

"Result 1" shows a polynucleotide that is 49 nucleotides long. SEQ ID NO:400 is 51 nucleotides long (*See* the ClustalW alignment of SEQ ID NO:400 with the "'060 app." sequence shown in Exhibit B, attached). The complement to SEQ ID NO:400 must be 51 nucleotides long. Claim 29 does not read on a polynucleotide complementary to SEQ ID NO:400, but the complement of SEQ ID NO:400. which, according to common usage of one of ordinary skill in the art, would have to have the same number of nucleotides as SEQ ID NO:400. Therefore, Applicants request that this rejection be withdrawn.

## CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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